Are All Hosts Created Equal? Partitioning Host Species Contributions to Parasite Persistence in Multihost Communities

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Cover Letter

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Re: ms 56086R1

The Editor, *the American Naturalist*

Thank you for accepting our article '*Are all hosts created equal? partitioning host species contributions to parasite persistence in multi-host communities*' for publication in The American Naturalist. We now upload the final version of the manuscript and figures, and we confirm that the relevant data have been archived in Dryad. I will also forward the relevant publication forms, as requested.

I hope everything is in order – please let me know if you need anything else at this stage.

Yours sincerely

Prof Andy Fenton

ARTICLE

Are all hosts created equal? Partitioning host species contributions to parasite persistence in multi-host communities

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Abstract

Many parasites circulate endemically within communities of multiple host species. To understand disease persistence within these communities it is essential to know the contribution each host species makes to parasite transmission and maintenance. However, quantifying those contributions is challenging. We present a conceptual framework for classifying multi-host sharing, based on key thresholds for parasite persistence. We then develop a generalised technique to quantify each species' contribution to parasite persistence, allowing natural systems to be located within the framework. We illustrate this approach using data on gastrointestinal parasites circulating within rodent communities and show that, although many parasites infect several host species, parasite persistence is often driven by just one host species. In some cases, however, parasites require multiple host species for maintenance. Our approach provides a quantitative method for differentiating these cases using minimal reliance on system-specific parameters, enabling informed decisions about parasite management within poorly understood multi-host communities.

Introduction

Parasites typically infect multiple host species (Begon 2008; Cleaveland et al. 2001; Pedersen et al. 2005; Rudge et al. 2013; Woolhouse et al. 2001), with important consequences for their spread to, and impact on, alternative host species. Indeed, many of the most pressing concerns about emerging infectious disease in humans [e.g., pandemic influenza (Kuiken 2006), West Nile virus (Kilpatrick *et al.* 2006)] and wildlife [e.g., bovine TB in cattle and badgers (Krebs et al. 1998), squirrel pox in red squirrels (Tompkins et al. 2002)] arise through transmission from one host species to another. More broadly, parasites often circulate endemically within 'reservoir' host communities, comprised of multiple host species (Haydon et al. 2002; Viana et al. 2014) which differ in their susceptibility, infectiousness and behaviour. Hence, host community composition, and the network of transmission among species, play a vital role in driving disease transmission and persistence at the community level (Fenton and Pedersen 2005; Haydon et al. 2002; Keesing et al. 2006; Kilpatrick et al. 2006; LoGiudice et al. 2003; Streicker et al. 2013).

To aid our understanding of multi-host parasite systems, a range of general theory has been developed (Begon 2008; Begon et al. 1992; Bowers and Begon 1991; Bowers and Turner 1997; Dobson 2004; Fenton and Pedersen 2005; Greenman and Hudson 1999; Greenman and Hudson 2000; Haydon et al. 2002; Holt et al. 2003; Holt and Pickering 1985). This body of theory shows that a parasite can only persist if its basic reproduction number across the whole community (denoted here as $R_{0,TOT}$) exceeds 1 (Dobson 2004). R_0 (or $R_{0,TOT}$) is formally a measure of the ability of a parasite to invade a completely naïve host population (or community), being able to do so if $R_0 > 1$. While it is true that stochastic forces may be important, particularly around this threshold value (i.e., parasites may fadeout if R_0 is slightly greater than 1, or may persist considerably if R_0 is slightly less than 1; (Fenton and Pedersen 2005; Lloyd-Smith et al. 2009; Lloyd-Smith et al. 2005)), in the deterministic models

described above $R_0 > 1$ is a requirement for the parasite to be maintained endemically, thereby providing an intuitive criterion for parasite eradication (by driving $R_0 < 1$). We therefore use the criterion $R_{0,TOT} > 1$ as our threshold for parasite persistence within a host community.

Importantly, the magnitude of $R_{0,TOT}$ will depend on the competencies of the different host species in the community, and the rates of between- and within-species transmission. These ideas are exemplified by the graphical framework developed by Holt and colleagues (Holt *et al.* 2003), which elegantly illustrates how different combinations of host species' densities combine to determine whether the parasite persists or not. This framework provides a valuable conceptualisation of the qualitative relationship between host abundance and parasite establishment or extinction. Such conceptual frameworks though do not, in themselves, provide a means to quantify the contributions of each host species to $R_{0,TOT}$ for genuine host-parasite systems. Hence, they do not enable quantification of the importance of each host species for the endemic persistence of a parasite, or provide quantitative predictions about the targeting of control measures towards each host species that drive $R_{0,TOT} < 1$.

Quantifying host species contributions to $R_{0,TOT}$, and predicting their consequences for parasite maintenance and the impact of control is highly challenging. Determining the species origin of infections (who infects whom) in a multi-host community using molecular tools has been possible in only a few host pathogen systems in which cross-species transmission is relatively rare (e.g., Streicker *et al.* 2010). Furthermore, experimental manipulations of host density or cross-species transmission, which could provide insight into host species contributions to parasite persistence, are rarely undertaken for logistical reasons (Bielby et al. 2014; Donnelly et al. 2003; Viana et al. 2015). As such there is a need to develop analytical tools that can make inferences about host contributions to parasite transmission and persistence from observational data. Recently, methods have been developed that do this for

certain multi-host disease systems (Funk et al. 2013; Rudge et al. 2013). For example, Rudge *et al*. (2013) presented an analysis which quantified host species contributions to $R_{0,TOT}$ of the human schistosome parasite *Schistosoma japonicum*. Using a system-specific transmission model, parameterised from values in the literature and observed infection prevalences, Rudge *et al*. were able to partition contributions to $R_{0,TOT}$ by a range of potential host species, allowing identification of those species that were most likely maintaining this parasite. Likewise, Funk *et al*. (2013) developed a similar approach for Human African Trypanosomiasis, showing that human infections were unlikely to be maintained without input from the animal reservoir. These studies required accurate estimates of various parameters for their system-specific models (e.g., mortality rates, recovery rates etc), which was facilitated by the detailed information available about those well-studied systems. However, such information is lacking for most parasites. For those species it would be invaluable to be able to make quantified inferences about likely levels of host contributions to $R_{0,TOT}$, based purely on easily-obtainable, standard parasitological data. Here we generalise the approach of Rudge *et al*. and Funk *et al*. to develop a flexible, generic method for readily estimating host species contributions to $R_{0,TOT}$, that can be applied across a range of multi-host – parasite systems with minimal reliance on system-specific parameter estimates.

In what follows, we first modify the conceptual framework of multi-host contributions to parasite persistence developed by Holt *et al*. (2003) to express their density-based axes in terms of host contributions to R_0, and formally categorise different types of multi-host dynamics based on key thresholds in this multi-dimensional R_0 space. Second, we generalise the system-specific approaches of Rudge *et al*. (2013) and Funk *et al*. (2013), to allow host species contributions to $R_{0,TOT}$ to be directly quantified. Third, we show how we can use the quantified contributions to $R_{0,TOT}$ to assess the proximity of an empirical system to the different thresholds for parasite persistence, and estimate likely responses to targeted

control strategies. Finally, we illustrate this process using a dataset of eight different parasite species circulating within communities of four potential host species. We emphasize that although variations on the two primary aspects of this work (a conceptual multi-host framework and an analytical method of quantifying host contributions to $R_{0,TOT}$) have previously been developed, they have remained largely independent of each other. We see great value in bringing these different approaches together. Specifically, their combination provides a powerful tool with which to (i) make quantified inferences about host contributions to a parasite's $R_{0,TOT}$ using easily-obtainable data, (ii) categorise the way parasites use the available host community, by locating the empirical system directly within the conceptual framework, and (iii) use this information to make quantitative predictions about the effects of targeted control, based on the proximity of the system to thresholds for disease eradication. This unified approach is crucial for wildlife systems, where accurate data on infection parameters are difficult to obtain, but understanding host contributions to parasite persistence is a vital conservation concern.

The multi-species theoretical framework

Our intention is to provide an intuitive, simple method of inferring host species contributions to parasite persistence using relatively easily obtained parasitological data. We therefore adopt a highly generic framework that is broadly applicable to both micro-parasites (e.g., viruses, bacteria etc) and macro-parasites (e.g., parasitic helminths). Specifically we model changes in the prevalence of infection in host species rather than, for example, modelling infection intensities, which are less easy to parameterise and can suffer greatly from problems of sampling error (Barbour 1996; Rudge et al. 2013); we return to this point in the Discussion. Here we first consider the case of homogenous transmission among host species;

later we extend it to allow for heterogeneities in the rates of transmission within and among host species.

The 'homogenous transmission' framework

We consider a parasite species circulating within a community of *n* host species of abundance H_i ($i = 1, 2 \ldots n$). For simplicity we assume these host species do not directly interact with each other (e.g., through competition) and so the presence or abundance of one species does not affect the presence or abundance of another species; such interactive scenarios have been considered in previous multi-host – parasite models (Bowers and Turner 1997; Greenman and Hudson 2000; Holt and Pickering 1985). Here we assume the parasite is transmitted via a single homogenous pool of infective stages (E) in the environment (e.g., spores, eggs, larvae, virions etc.; Fig. 1A), although a similar framework is easily developed for directly-transmitted parasites (see Online Appendix). The dynamics of the system are given by:

$$\frac{dP_i}{dt} = (1 - P_i)\beta_i E - b_i P_i \qquad \text{Eq. 1a}$$

$$\frac{dE}{dt} = \sum_{i=1}^{n} \lambda_i P_i H_i - \gamma E, \qquad \text{Eq. 1b}$$

where P_i is the prevalence of infection in host species i, β_i is the transmission rate to host species i, b_i is the loss rate of infected individuals of host species i (incorporating recovery, and natural and parasite-induced mortality), λ_i is the rate of infective stage production by infected individuals of host species i (here assumed to be independent of infection intensity; Rudge et al. 2013) and γ is the mortality rate of infective stages in the environment. For simplicity, we assume the loss rate of infective stages from the environment through uptake by hosts is negligible; relaxation of this assumption would reduce the parasite's overall R_0, but would require explicit information about the rate of uptake in order to quantify, which

may be very hard to obtain. Hence we ignore this possibility in what follows. Following the next generation method of Diekmann & Heesterbeek (2000), the parasite's overall basic reproduction number in the community of *n* host species is given by the dominant eigenvalue of the transmission matrix (Dobson 2004; see also Rudge et al. 2013):

$$R_{0,TOT} = \sqrt{\sum_{i=1}^{n} R_{0,i}} \qquad \text{Eq. 2.}$$

where $R_{0,i} = \beta_i \lambda_i H_i / \gamma b_i$, corresponding to the parasite's R_0 value when host *i* is the only species in the community. Hence, when all hosts have equal access to a common pool of infective stages (Fig. 1A), the parasite's overall basic reproduction number within the whole host community is simply proportional to (specifically, the square root of) the sum of the individual $R_{0,i}$ for each host species alone.

From this theoretical basis, we can modify the framework of Holt *et al.* (2003) to illustrate how the contributions of each host species combine to determine the parasite's overall $R_{0,TOT}$; here we do that for two host species (i=1,2; Fig. 1B) although the concepts apply to any number of host species. The different possible thresholds of disease persistence given by the $R_{0,i} = 1$ and $R_{0,TOT} = 1$ result in five regions of parameter space:

Region 1: the parasite cannot persist ($R_{0,TOT} < 1$). The upper boundary of this region is given by the equation $R_{0,TOT} = 1$ and, due to the assumption of shared access to a common transmission pool (see later where this is relaxed), the two host species combine additively to determine the parasite's overall basic reproduction number (Eq. 2), and this boundary is the straight diagonal from $R_{0,1} = 1$ to $R_{0,2} = 1$ (Fig. 1B). This is equivalent to the 'substitutable' hosts of Holt *et al.* (2003).

Region 2: the parasite is maintained solely by host species 1 (the reservoir or 'maintenance' host in the terminology of Haydon et al (2002); $R_{0,1} > 1$), but causes spillover

infections in host species 2, which contributes little to parasite persistence and is unable to maintain the parasite on its own ($R_{0,2} < 1$).

Region 3: the reverse of Region 2, with species 2 being the maintenance host and species 1 the spillover host ($R_{0,2} > 1$ and $R_{0,1} < 1$).

Regions 4 and *5* represent cases where infection is observed in both host species, but through very different processes. In *Region 4* (which we term 'facultative multi-host parasitism') either host species can maintain the parasite alone ($R_{0,i} > 1$ for $i = 1,2$) whereas in *Region 5* ('obligate multi-host parasitism') the parasite needs both hosts in order to persist ($R_{0,i} < 1$ for $i = 1$ and 2, but $R_{0,TOT} > 1$).

Clearly, where a parasite lies within this framework will greatly alter the impact of control measures targeting either host species (Fenton and Pedersen 2005). As such, if the individual species' contributions to $R_{0,TOT}$ (the $R_{0,i}$) can be empirically quantified, then it will be possible to determine which region a given host-parasite community resides in, and make quantitative predictions regarding the control effort and targeting of particular host species required to shift the community below the threshold for disease persistence. Below we describe an approach that can allow this. However, first we extend the framework to allow for more realistic transmission pathways among host species.

Improving the framework: allowing for heterogeneous sharing of infective stages

The 'homogenous transmission' framework above assumes that all hosts are exposed to a single, homogenous pool of parasite infective stages. In reality however, this is unlikely to be the case. For environmentally-transmitted parasites for example, if different host species occupy relatively distinct spatial locations, infective stages released from one host will be more likely to be picked up by an individual of the same species than the other species, giving rise to incomplete transmission overlap, or 'assortative transmission'. This will result

in within-species transmission being greater than between-species transmission, thereby altering the overall R_0 and the relative contributions of the different species. Note that the methods we present can allow for disassortative transmission, where there is more between-species transmission than within (see Holt *et al*. (2003) for a consideration of this case); however, we consider it less likely and so do not explicitly consider here.

To model heterogeneous sharing of infective stages we describe two distinct pools of infective stages in the environment, one (E_1) comprising infective stages released by host species 1, and the other (E_2) released by host species 2 (Fig. 2A). Both species have access to either pool of infective stages, with infection occurring at rate β_{ij}, describing the rate at which host species *i* picks up infective stages released by host species *j* (in the case where *j* = *i*, this becomes β_{ii}, representing the rate of within-species transmission). The dynamics of the system are then given by:

$$\frac{dP_i}{dt} = (1 - P_i)\beta_{ii}\left(\sum_{j=1}^{n} \omega_{ij} E_j\right) - b_i P_i \qquad \text{Eq. 3a}$$

$$\frac{dE_i}{dt} = \lambda_i P_i H_i - \gamma E_i, \qquad \text{Eq. 3b}$$

where $\omega_{ij} = {\beta_{ij}}/{\beta_{ii}}$ is a measure of the degree of between-species transmission experienced by host species *i* relative to its rate of within-species transmission (see Rudge *et al*. (2013) for description of a specific formulation for a parasite with an intermediate host stage). If $\omega_{ij} < 1$ then host species *i* is more likely to become infected by infective stages released from individuals of its own species than those of the other species (between-species transmission is less than within-species transmission). However, if $\omega_{ij} = 1$ then the host is just as likely to encounter parasites released from either species (cross-species transmission equals within-species transmission), and we recover the homogenous model (Eqs 1a,b, with $E = \sum_{i=1}^{n} E_i$). In what follows we ignore the (perhaps rare) possibility that hosts are more likely to

encounter infective stages released from a different host species than its own ($\omega_{ij} > 1$). We also ignore the possibility that $\omega_{ij} < 0$ as a phenomenological representation of the dilution effect, where one species interferes with transmission to the other. A more accurate representation of this process would require explicit measurement of the rate of uptake of infectious stages from the environment, something that would be hard to quantify, so we do not consider it further here. Finally, note that the relative rates of cross-species transmission need not be symmetrical ($\omega_{ij} \neq \omega_{ji}$), for example if the territory of species *i* is completely embedded within the territory of species *j* then species *i* may be just as likely to encounter infective stages released from either host species ($\omega_{ij} \sim 1$) whereas species *j* may only rarely encounter infective stages from species *i* ($\omega_{ji} \ll 1$).

Incorporating assortative transmission alters how the host species combine to determine the parasite's overall R_0. Again, following the next generation method of Diekmann & Heesterbeek (2000), the parasite's overall basic reproduction number within a community of two host species is now:

$$R_{0,TOT} = \frac{1}{2}\left[R_{0,1} + R_{0,2} + \sqrt{\left(R_{0,1} + R_{0,2}\right)^2 - 4R_{0,1}R_{0,2}(1-\omega)}\right] \qquad \text{Eq. 4,}$$

where $\omega = \omega_{12}\omega_{21}$. Deriving an analytical expression for $R_{0,TOT}$ is more difficult, or even impossible, for more than two host species, but numerical solutions can readily be found (Dobson 2004). Now, unlike the case of homogenous mixing previously (Eq. 2), the contributions from each host species do not combine additively to determine $R_{0,TOT}$. Furthermore, if $\omega < 1$ then the boundary separating the region where the parasite cannot persist, and the region where it can only persist in the presence of the two host species, bows outward (Fig. 2B; see also Bowers and Turner (1997)). Here the system becomes equivalent

to the 'weakly interacting hosts' scenario of Holt *et al.* (2003), showing that assortative transmission makes it less likely for a community of host species with $R_{0,i} < 1$ to maintain the parasite. In the limit when $\omega = 0$, the region of parasite extinction completely excludes the 'obligate multi-host' region, and it is no longer possible for two host species each with $R_{0,i} < 1$ to combine to maintain the parasite, due to the lack of transmission between them (the 'noninteractive hosts' scenario of Holt *et al.* (2003); see also (Begon et al. 1992; Bowers and Turner 1997; Holt and Pickering 1985)). The remaining regions in Fig. 2B are identical to those in the homogenous transmission framework (Fig. 1B).

Locating host-parasite systems within the multi-host framework

To quantify the contributions of each host species to overall R_0 of a given parasite, and locate it within the above conceptual framework, we generalise the approach of Rudge *et al.* (2013) and Funk *et al*. (2013) to describe a generic environmentally-transmitted parasite. As in their approach, we quantify the host species contributions using a prevalence-based framework, such as the one presented in Eqs 3a,b, assumed to be at steady state (although results appear robust to deviation from this assumption; see Discussion for details). However, instead of having to estimate each parameter in the model independently, we estimate the $R_{0,i}$ directly. Specifically, by assuming the system is at equilibrium we set Eqs 3a,b equal to zero and rearrange to give:

$$R_{0,i} = \frac{1}{(1-P_i^*)\sum_{j=1}^{n}(\delta_{ij}\varepsilon_{ij}\upsilon_{ij}\omega_{ij})} \qquad \text{Eq. 5}$$

where, as before, $R_{0,i} = \beta_{ii}\lambda_i H_i/\gamma b_i$, and P_i^* is the prevalence of infection in host species i, $\delta_{ij} = {\lambda_j}/{\lambda_i}$, $\varepsilon_{ij} = {H_j}/{H_i}$, $\upsilon_{ij} = {P_j^*}/{P_i^*}$ and $\omega_{ij} = {\beta_{ij}}/{\beta_{ii}}$. The infection prevalence can

typically be measured, or at least estimated, for most host-parasite systems, as can the relevant variables for the δ_{ij}, ε_{ij} and υ_{12} composite parameters (host abundance, H_i, and the release of parasite infective stages per infected host, λ_i). Furthermore, if there is complete overlap of transmission between the host species (cross-species transmission equals within-species transmission, $\omega_{ij} = 1$), the contribution of each host species to the parasite's overall R_0 can be fully quantified, allowing the system to be placed directly within the multi-host framework (e.g., Fig. 1B).

In the case of heterogeneous transmission the quantification must account for $\omega_{ij} \neq 1$. In some cases it might be possible to use natural history observations as a proxy for the degree of transmission overlap among host species, for example the observed degrees of home range overlap among the different species or degree of spatial correlation among species (e.g., Funk et al. 2013). In the absence of such information, one can investigate how uncertainty in the value of ω_{ij} affects the estimated $R_{0,i}$, by sampling across a plausible range of values for each of the ω_{ij} (e.g., Rudge et al. 2013). This procedure then asks, what level of $R_{0,i}$ is needed to generate the observed prevalence in that host species under different degrees of input (cross-species transmission) from the other host species? Clearly, if there is little input from the other host species ($\omega_{ij} \sim 0$) then $R_{0,i}$ must be relatively high in order to generate the observed prevalence in host species i. Conversely, if there is complete transmission overlap ($\omega_{ij} = 1$) then $R_{0,i}$ is likely to be low. In the next section we illustrate this process using empirical data for eight parasite species within their host communities of up to four host species.

Empirical illustration of the framework

Description of empirical system

We collected data on small mammal (*Rodentia*) community composition and gastrointestinal parasite occurrence across 19 grids in six sites in Virginia, Tennessee, New York and Connecticut (see Streicker *et al.* 2013 for details). Animals were captured for two to three consecutive nights at each site and fecal samples were collected from Sherman live traps to identify gastrointestinal parasites and quantify parasite egg/oocyst shedding rates. We present results for the eight most common parasite species or pseudo-species (two nematodes, three cestodes and three coccidia species) for which we have the greatest confidence in identification. We acknowledge limitations in this dataset that would have to be overcome in order to make predictions for disease systems of more practical concern (e.g., the need for accurate parasite identification, ideally using molecular techniques, and longer-term sampling to accurately quantify prevalence). We therefore emphasize that we use these data purely as a convenient means to illustrate the application of the approaches described here. The data are deposited in the Dryad Digital Repository: http://dx.doi.org/10.5061/dryad.972mv (Fenton *et al.* 2015).

Estimating host species' contributions to R_0 from our empirical data

For each parasite species we used Eq. 5 to calculate the host species-specific contributions to the parasite's basic reproduction number ($R_{0,i}$) using empirical data on species-specific patterns of abundance, parasite shedding and prevalence of infection. To assess uncertainty in the contribution of each host species under different cross-species transmission scenarios, we calculated $R_{0,i}$ using a series of values of ω_{ij} ranging from 0 (no between-species transmission) and 1 (equal between- and within-species transmission) in steps of 0.01 (Fig. 3 coloured dots; the mean values of those 100 calculations is denoted by the cross, with error bars showing 2.5% – 97.5% quantiles). Note this procedure assumes complete symmetry in overlap among all the hosts ($\omega_{ij} = \omega_{ji}, \forall_{i,j}$), so we repeated the process drawing all ω_{ij}

values at random from a uniform distribution between 0 and 1 (thereby allowing $\omega_{ij} \neq \omega_{ji}$; Fig. A1, red dots). However, there was very little difference in the subsequent predicted values of $R_{0,i}$ (compare Fig. 3 with Fig. A1) so we focus here on the results of the former procedure. In what follows, given the variation in predicted $R_{0,i}$ values (arising from the variation in ω_{ij} values), we classify contributions of each host species depending on whether the majority of $R_{0,i}$ values are greater or less than 1.

Across the eight parasite species we found a range of host-sharing scenarios (Fig. 3). Four parasite species (*Eimeria* A, *Eimeria* B, *E. delicata* and *C. americana*) clearly had one dominant host species with individual $R_{0,i}$ values greater than 1, and substantially greater than that of the other host species in the community, almost regardless of the values of ω_{ij}; in these cases the dominant host is an obvious maintenance host even in the absence of any other host species. For two of those species (*Eimeria* A and *Eimeria* B), there was evidence that a second host species could also be making a significant contribution to overall parasite maintenance, depending on the values of the ω_{ij}. Indeed, under some values of transmission overlap (particularly when ω_{ij} was very small; Fig. 3 red points), the estimated $R_{0,i}$ values for these 'secondary' hosts often exceeded 1, suggesting they could be maintenance hosts in their own right. Finally, for *Hymenolepis* A, it appears unlikely that any of the host species alone would be able to maintain the parasite under most scenarios of transmission overlap ($R_{0,i} < 1$ for all host species); hence, under the assumptions of our model, and with the quality of data available to us, it seems this parasite may require multiple host species to be maintained (i.e., it is an obligate multi-host parasite).

Fig. 4 locates each of these parasites within the 2-dimensional $R_{0,1} - R_{0,2}$ framework for the top two contributing host species for each parasite (the dominant host species is plotted on the x-axis in each case; note we assume transmission heterogeneity is not constrained ($\omega_{ij} \neq \omega_{ji}$) for full characterization of uncertainty). Many parasite species

(*Eimeria* B, *E. delicata*, *A. americana*, *C. americana*) appear to show spillover dynamics, occupying the lower right-hand quadrant of Fig. 4, while two parasite species (Cestode A and *Hymenolepis* B) lie on the border with the region of obligate multi-host parasite. In all these cases there is a clear maintenance host species, with the other host(s) being unable to maintain transmission alone, suggesting that targeted removal of the maintenance host would eradicate the parasite from the community (assuming no compensatory growth by the remaining species in the community post-removal). For two species (*Eimeria* A and possibly *Eimeria* B) there is evidence that these species may be facultative multi-host parasites (lying towards the top right hand region of Fig. 4), depending on the precise network of transmission (i.e., the ω_{ij} values) among the host species. If so, this would suggest these parasite species can be maintained by more than one host species alone. Finally, *Hymenolepis* A seems to sit firmly within the region of being an obligate multi-host parasite, suggesting it cannot be maintained by any single host species alone (assuming no compensatory growth in host abundance), but requires transmission among multiple host species in order to be maintained. Note that, for this species, the top two hosts only contribute ~80% of $R_{0,TOT}$, highlighting that there is a third host species making a not-insignificant contribution to transmission (Fig. 3).

Predicted impact of targeted control

The above section illustrates how placing host species contributions to $R_{0,TOT}$ within the framework provides an intuitive appreciation of how host community configuration affects parasite persistence. Here we extend those insights to make specific predictions about the likely consequences of control for parasite persistence and prevalence. We use Eq. 5, parameterised with the estimated values of $R_{0,i}$ for each parasite species to calculate the resulting equilibrium prevalence (the P_i^*) for the remaining host species in the community

following targeted control (e.g., treatment or culling) of the host species with the highest initial number of infected individuals. Control is assumed to be 100% effective, such that contribution to parasite transmission from the targeted host species is completely blocked. Note, we assume that the imposed control does not alter the abundances of the remaining host species in the community (the H_i are unchanged from pre-control levels). Clearly the effect of targeted control would be altered if remaining host species increased following control. For example, as shown by Bowers and Turner (1997), competition between hosts could suppress combined densities sufficiently to keep $R_{0,TOT} < 1$, such that the system sits in the 'parasite extinction region' (Fig 2B); in this scenario removal of one of the host species may then allow the remaining species to increase sufficiently to drive $R_{0,TOT} > 1$, allowing the parasite to persist (see also Begon 2008). This interplay between competition and community $R_{0,TOT}$ could be incorporated within the present framework by allowing the remaining species to increase in abundance following removal of the target host species, based on estimated or hypothesised competition coefficients among species (Begon 2008; Bowers and Turner 1997; Greenman and Hudson 2000; Holt and Pickering 1985). However, for simplicity we ignore this possibility here.

Overall, the previous intuitive predictions about the consequences of targeted control were upheld by this quantitative analysis; removal of the dominant host species (those marked with the '*' in Fig. 5) was nearly always predicted to bring about elimination of the parasite in the remaining host community (Fig. 5). In most cases, infection persisted only when transmission overlap was negligible ($\omega_{ij} \sim 0$, such that each host species maintains infection in virtual isolation from other hosts). However, there was strong evidence to suggest that *Eimeria* A infection could be maintained by *P. maniculatus* even in the complete absence of the dominant host *P. leucopus*. Hence this parasite species appears to be something of a 'facultative multi-host parasite', able to infect and be maintained on more than one host

species. Furthermore, there was some evidence that *Eimeria* B, and possibly *Hymenolepis* A, was able to persist in the absence of the dominant host species, but only if transmission overlap was low ($\omega_{ij} \to 0$), such that those secondary host species were able to maintain infection in relative isolation.

Discussion

Understanding the spread of parasites and pathogens through multi-host communities, and quantifying the contributions each host species makes to the transmission, persistence and abundance of parasites within those communities, remain major challenges in the management of infectious diseases. To address these challenges we first modified an existing conceptual framework (Holt *et al.* 2003) to provide an intuitive method for classifying different kinds of parasite host-sharing within empirical multi-host communities, based on host contributions to the parasite's overall basic reproductive number across the host community ($R_{0,TOT}$). This framework clearly delineates parasites which show spillover dynamics (maintained by one key host) from those that either require multiple host species in order to persist, or those that can persist on any of several host species. Importantly, we show how we can use this not just as a conceptual framework, but as a practical tool in evaluating host species contributions to parasite persistence. Specifically, we combined this framework with a generalised analytical approach (modified from the system-specific approach presented by Funk et al. 2013; Rudge et al. 2013) and showed how to quantify host-species contributions to a parasite's community-level R_0, infer proximity of the system to important thresholds of parasite persistence/eradication, and predict the community-wide outcomes of targeted control, all using readily-collected parasitological data. Together, this combination of approaches provides a powerful method of identifying optimal management approaches

for circulating diseases within natural ecological communities, where detailed understanding of system dynamics is rarely available.

One of the biggest challenges with understanding the movement of parasites through multi-host communities is estimating the rates of between-species transmission relative to within-species transmission. We characterised these relative rates in terms of the degree of 'transmission overlap' between the host species, described by the ω_{ij} terms. However, estimating this overlap for natural communities is not straightforward. Assuming such heterogeneous transmission arises primarily from spatial segregation of host species, it may be possible to infer likely degrees of transmission overlap from measures of home range overlap or habitat usage between species (Carslake et al. 2006; Funk et al. 2013). Alternatively, analysis of parasite sequence data from across the host community could reveal likely rates of cross-species transmission (Biek et al. 2012; Streicker et al. 2010). If these approaches are not possible, it would be necessary to sample values of ω_{ij} across the feasible range, as we have done here, to assess uncertainty in parameter estimates (e.g., Rudge et al. 2013). Regardless of how it is done, estimating this transmission overlap can be important, as it affects both the boundary for parasite persistence (Fig. 2; see also Holt *et al*. (2003)) and the estimated values of species-specific contributions to $R_{0,TOT}$ (estimated $R_{0,i}$ values increase as ω_{ij} decreases; Fig. 3). Notably however, for many of the communities analysed here, uncertainty in the degree of transmission overlap did not greatly alter either the location of the system within the multi-host framework (Fig. 4) or the predicted consequences of targeted control (Fig. 5). Indeed, although the circulation of parasites within these ecological communities appears highly complex, the dynamics of transmission in most cases appeared to be driven by just one host species. Studies of other multi-host communities suggest similarly that often there is a dominant, key host responsible for the majority of transmission of the focal parasite or pathogen (e.g., Kilpatrick et al. 2006; Lembo et al. 2007; LoGiudice et

al. 2003; Roeder et al. 2013). Hence, it may be that much of the apparent complexity of many multi-host systems could reasonably be simplified to focus on one or two key components of the community. Clearly there will be exceptions to this (e.g., *Eimeria* A and *Eimeria* B in the present study), where it appears the parasite could be maintained by secondary species in the absence of the dominant species. Importantly, the approaches described here provide a clear, quantitative method for differentiating these cases.

The accuracy of the quantitative predictions will obviously depend greatly on the quality of the data available. Of crucial importance is to ensure accurate identification of parasite species across the different host species, ideally using molecular techniques, to distinguish true multi-host parasites from multiple apparently similar host-specific species (Streicker et al. 2010). Furthermore, it is essential that sampling errors and biases are minimised, or at least quantified. For example, accurately quantifying infection status can depend greatly on the sensitivity and specificity of the diagnostic method used; hence, Rudge *et al*. (2013) used a Bayesian framework to quantify 'true' prevalence, given uncertainties in the diagnostic tests. Such problems are magnified when attempting to quantify infection burdens (e.g., for parasitic helminths), making parameterisation of intensity-based models highly problematic, and tending to result in under-estimation of R_0 (Barbour 1996). We therefore used a prevalence-based framework which, although ignoring heterogeneity in infection burdens, provides a more robust framework for quantifying transmission, and is often used to aid parameterisation of helminth models from field data (Gray et al. 2008; Hairston 1965; Ishikawa et al. 2006; Montresor et al. 2013; Rudge et al. 2013; Williams et al. 2002). Explicitly incorporating infection intensities is not possible within the current framework, and so the consequences of relaxing this assumption are unclear. However this issue could be explored either using a classic host-macroparasite framework, where the degree of parasite aggregation is imposed on the system (Anderson and May 1978), or an

individual-based framework where it emerges dynamically (e.g., Fenton et al. 2010). Finally, it is important to consider sampling biases, particularly in the estimation of host abundances, where different host species may have different probabilities of being sampled (e.g., trap success varies between species), or infection status may influence capture success (e.g., if infected animals are more/less likely to be caught than uninfected animals). Similar to the adjustment described in Streicker *et al*. (2013), if estimates of *per capita* trap probability for each species are available, they could be used to correct the observed host abundances in Eq. 5 (contained within the ε_{ij} terms). If such estimates are not available then uncertainty arising from possible differential capture success could be incorporated by repeatedly sampling from a plausible distribution (Streicker *et al.* 2013).

Related to the above considerations, one key assumption we make is that the system is at equilibrium. Although it is unlikely that many natural systems are truly at equilibrium, they may not be far from it, and results may be relatively insensitive to deviations from this assumption. To assess the extent to which our estimated $R_{0,i}$ values are affected by this assumption we ran a series of simulations of a hypothetical two-host community (see Online Appendix for details) in which we allowed the abundance of each host species to fluctuate around a mean value, either stochastically (Fig. A2), or regularly (to mimic seasonal or periodic cycles in abundance), with the host species either cycling out of phase with each other (Figs A3, A4) or in phase (Fig. A5). Overall, the estimated $R_{0,TOT}$ values and the estimated ratio of the $R_{0,i}$ values did not differ greatly from the 'true' values in the models, even for large amplitude fluctuations in host abundance (Figs A2-A3), and even if there were asymmetries in the extent of transmission overlap between the species (Fig. A4). Only when host species underwent large-amplitude fluctuations completely in phase with each other did the estimated values begin to differ significantly from the true values (Fig. A5). Clearly this sensitivity analysis is not exhaustive and there may be conditions under which the estimated

values depart significantly from the 'true' values. However, we suggest that our approach is relatively robust to the assumption of being at steady state. Crucially though this depends greatly on the accuracy of estimates of host abundance, a vital input parameter for the calculation (Eq. 5). For this reason we would suggest snap-shot estimates of abundance are unlikely to be sufficient, so long-term data on host abundances should be used where possible. In systems where the equilibrium assumption might to lead to significant errors in estimation, values of $R_{0,i}$ could be estimated by applying contemporary model fitting techniques to long-term time series data on host abundances and infection prevalences (e.g., Ionides *et al.* 2006; Shrestha *et al.* 2013).

There is currently great appreciation of the community context of disease. Many parasites and pathogens of human health, economic or conservation importance circulate within multi-host reservoir communities. Without an understanding of how parasites flow within and between host species in these communities it is impossible to anticipate disease emergence from them, or assess how shifts in those communities (e.g., arising from host species losses or gains associated with land use change, climate change or human management) will affect disease risk and occurrence within them. The approaches we have described provide an intuitive and accessible means to quantify the contributions that individual host species make to parasite transmission and persistence, thereby providing a quantitative basis from which to make informed decisions about the management of multi-host parasites.

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1) Application to directly-transmitted (micro)parasites

The framework presented in the main paper specifically describes an environmentally-transmitted parasite. However, the principles can readily be adopted to cover a range of different parasite types; here we illustrate that with reference to a directly-transmitted parasite (i.e., one that infects by close contact between susceptible and infected individuals). This model and subsequent framework very closely matches that of Holt *et al*. (2003) and related theory (Begon 2008; Begon et al. 1992; Bowers and Turner 1997; Dobson 2004; Holt and Pickering 1985), and we present it here to highlight connection with that previous body of work, and to emphasise the generality of this approach.

As in the main paper, the prevalence of infection in each of *n* host species can be described by:

$$\frac{dP_i}{dt} = (1 - P_i)\left(\sum_{j=1}^{n} \beta_{ij} P_j H_j\right) - b_i P_i \qquad \text{Eq. A1}$$

where P_i is the prevalence in host species i, β_{ij} is the transmission rate from an infected individual of species j to a susceptible individual of species i, H_j is the abundance of host species j and b_i is the loss rate of infected individuals of species i (incorporating recovery and natural and parasite-induced mortality). The parasite's R_0 value when host i is the only species in the community is then $R_{0,i} = \beta_{ii} H_i / b_i$. Eq. A1 may be rewritten as:

$$\frac{dP_i}{dt} = (1 - P_i)\beta_{ii} P_i H_i\left(\sum_{j=1}^{n} \omega_{ij}\, \upsilon_{ij} \varepsilon_{ij}\right) - b_i P_i \qquad \text{Eq. A2,}$$

where $\omega_{ij} = {\beta_{ij}}/{\beta_{ii}}$ and, as in the main paper, $\varepsilon_{ij} = {H_j}/{H_i}$ and $\upsilon_{ij} = {P_j}/{P_i}$. As in the main paper, if we assume the system is at equilibrium, Eq. A2 may be rearranged to give:

$$R_{0,i} = \frac{1}{(1-P_i^*)\sum_{j=1}^{n}(\varepsilon_{ij}\upsilon_{ij}\omega_{ij})} \qquad \text{Eq. A3,}$$

corresponding to Eq. 5 in the main paper (see also Begon et al. 1992; Bowers and Turner 1997; Dobson 2004; Holt et al. 2003; Holt and Pickering 1985, for details on the dyanmics of systems similar to this). Hence the contributions of each host species to $R_{0,TOT}$ can be estimated based simply from measurements of host abundance and infection prevalence, with uncertainty due to cross-species transmission quantified by varying the ω_{ij}, as in the main paper.

2) Exploring the assumption of equilibrium dynamics

A key assumption in the paper is that the system is at equilibrium. To assess how sensitive our results are to that assumption, we ran a series of simulations of a 2-host system, where we allowed host abundances to vary. We modelled the system using either Eqs 1a and b from the main paper (assuming complete overlap in transmission; $\omega_{12} = \omega_{21} = 1$), or Eqs 3a and b (assuming heterogeneous transmission; $\omega_{12} \neq \omega_{21} \neq 1$), All other parameters were assigned fixed, arbitrary values. We then allowed the abundance of each host species to vary throughout each simulation around a constant mean value ($\bar{H}_1 = \bar{H}_2 = \bar{H}$) according to one of four scenarios:

1) H_1 and H_2 vary stochastically, independently of each other. Here, host abundances were drawn every integer time step (t=1, 2…) from a uniform distribution of amplitude δ, centred around $\bar{H}$. This amplitude parameter was increased each simulation from 0 (no fluctuation in host abundance, mimicking true equilibrium dynamics) to $\bar{H}$ (allowing fluctuation in host abundance between 0 and $2\bar{H}$).
2) H_1 and H_2 vary regularly, out of phase with each other, according to sine wave functions:

   $H_{1(t)} = \bar{H} + \delta \sin(t)$ and $H_{2(t)} = \bar{H} + \delta \sin(t + h)$

   where δ is the amplitude of fluctuation (assumed to be the same for host species 1 and 2), and h is the magnitude of the offset between species. As in scenario 1, δ was varied from 0 to $\bar{H}$.
3) H_1 and H_2 vary as in (2) above, but assuming asymmetrical, heterogenous transmission between the two host species ($\omega_{12} \neq \omega_{21} \neq 1$).

4) H_1 and H_2 vary regularly, in phase with each other. This was equivalent to scenario 2, but with h=0.

In each case we calculated the 'true' value of the $R_{0,i}$ over the simulation period (simulations were run for up to 100 time units, with the first 50 time units discarded) using $R_{0,i} = \beta_i \lambda_i H_i / \gamma b_i$, based on the observed mean value of the H_i (H_i^*) over the course of the simulation period. We then compared these 'true' values with the estimated values of the $R_{0,i}$ calculated from Eq. 6 (main paper), using the predicted mean prevalence values for the two host species (P_1^* and P_2^*) and observed mean host abundances (H_1^* and H_2^*) over the simulation period as input variables.

For both scenario 1 (stochastic fluctuations) and scenario 2 (regular, out-of-phase fluctuations), both the estimated $R_{0,TOT}$ values and the estimated ratio of the $R_{0,i}$ values closely matched the 'true' values, even for large amplitude fluctuations in host abundance (high δ values; Figs A2-A3). These findings were also relatively robust if the assumption of homogenous transmission was relaxed (Fig. A4). It was only when the host species underwent large-amplitude fluctuations in perfect phase with each other that the estimated values differed significantly from the true values (Fig. A5).

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Figure legends

Fig. 1. (A) Schematic diagram of the homogenous transmission model, assuming a single pool of parasite infection stages in the environment. (B) $R_{0,1} - R_{0,2}$ parameter space for the homogenous transmission model, showing the five regions of dynamic outcome: Parasite exclusion; Spillover ($H_1 \rightarrow H_2$); Spillover ($H_2 \rightarrow H_1$); Facultative multi-host ('M.H.'); Obligate multi-host.

Fig. 2. (A) Schematic diagram of the heterogeneous transmission model, where ω represents the degree of transmission overlap. (B) $R_{0,1} - R_{0,2}$ parameter space for the heterogeneous transmission model, showing the same five regions as in Fig. 1.

Fig. 3. Estimated $R_{0,i}$ values for each of the four host species for the eight parasite species in the dataset. The coloured points refer to the different values of ω_{ij} used for each calculation (colour coded from red: ω_{ij}=0 to blue: ω_{ij}=1; assumed to be symmetrical for all host species in the community; $\omega_{ij} = \omega_{ji}, \forall_{i,j}$). The crosses denote the mean $R_{0,i}$ across the different ω_{ij} values and the error bars represent 2.5% – 97.5% quantiles. The asterisks denote the dominant host species, based on number of infected individuals.

Fig. 4. $R_{0,1}$ - $R_{0,2}$ parameter space for the two dominant host species for each of the eight parasite species in the dataset. The points refer to the different values of ω_{ij} used for each calculation (assumed to vary between all host species pairs in the community; $\omega_{ij} \neq \omega_{ji}$). The crosses denote the mean $R_{0,i}$ across the different ω_{ij} values and the error bars represent 2.5% – 97.5% quantiles. The number in the top right of each plot denotes the proportion of $R_{0,TOT}$ explained by $R_{0,1}$ and $R_{0,2}$.

Fig. 5. Predicted prevalence of infection in the remaining host species in the community following 100% efficacy control of the dominant host species (denoted by the asterisks). The points refer to the different values of ω_{ij} used for each calculation (assumed to vary between all host species pairs in the community; $\omega_{ij} \neq \omega_{ji}$). The crosses denote the mean predicted prevalence across the different ω_{ij} values and the error bars represent 2.5% – 97.5% quantiles. The black bars show observed infection prevalence in the absence of control.

Online Appendix figure legends

Fig A1. Estimated $R_{0,i}$ values for each of the four host species for the eight parasite species in the dataset. This figure is analogous to Fig 3 in the main paper, except here it is not assumed that the degrees of transmission overlap are symmetrical for all host species in the community ($\omega_{ij} \neq \omega_{ji}, \forall_{i,j}$). The crosses denote the mean $R_{0,i}$ across the different ω_{ij} values and the error bars represent 2.5% – 97.5% quantiles. The asterisks denote the dominant host species, based on number of infected individuals.

Fig A2. Simulation results, assuming stochastic fluctuations in host abundance. Main figure: comparison of estimated (by Eq. 6; red line) and 'true' (black line) $R_{0,TOT}$ values (top panel) and $R_{0,1}/R_{0,2}$ values (bottom panel), with varying amplitude of fluctuation in host abundance (δ). The three inset figures along the top each show time series of (i) host abundance (top panel) and (ii) predicted parasite prevalence calculated by Eqs 1 and 2 in the main paper (bottom panel) for host species 1 (blue) and host species 2 (purple) for δ=0 (no fluctuation in abundance; left hand figure), δ=50 (medium fluctuation in abundance; centre figure) and δ=100 (extreme fluctuation in abundance). Model runs assume homogenous transmission

such that $\omega_{12} = \omega_{21} = 1$. Parameter values are: $\beta_1 = 0.005$, $\beta_2 = 0.002$, $b_1 = 1$, $b_2 = 1$, $\lambda_1 = 10$, $\lambda_2 = 10$, $\gamma = 2$, $\bar{H}_1 = \bar{H}_2 = 100$.

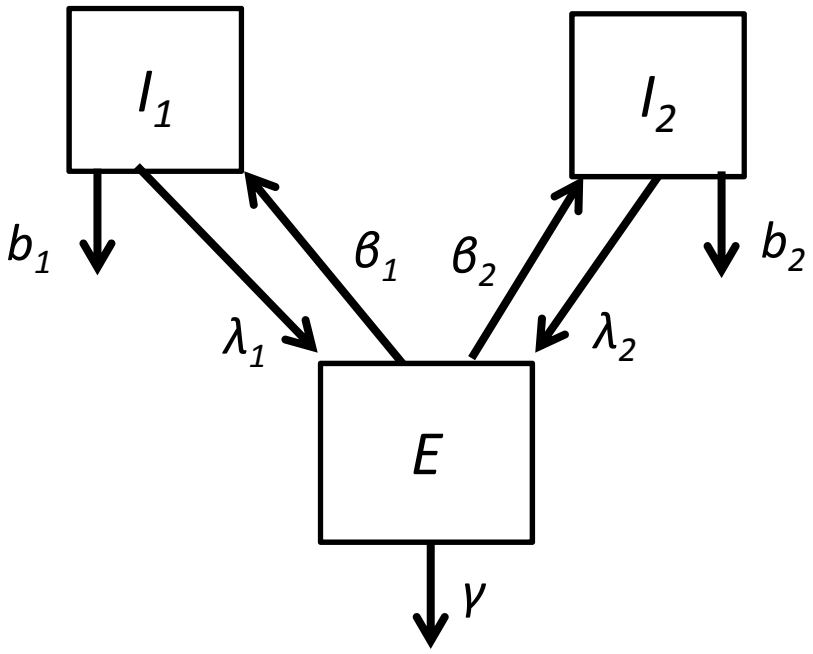
Fig A3. As in Fig. A2, but assuming regular fluctuations in host abundance, according to a sine function, with species 1 and 2 cycling out of phase with each other (h=10). All other parameter values are as in Fig. A2.

Fig A4. As in Fig. A3, but assuming asymmetrical, heterogeneous transmission between the two host species ($\omega_{12} = 0.5, \omega_{21} = 0.25$). All other parameter values are as in Fig. A2.

Fig A5. As in Fig. A3, but assuming host species fluctuate in phase with each other (h=0). All other parameter values are as in Fig. A2.

Fig 1

A)


I_1
I_2
b_1
β_1
β_2
b_2
λ_1
λ_2
E
γ

B)

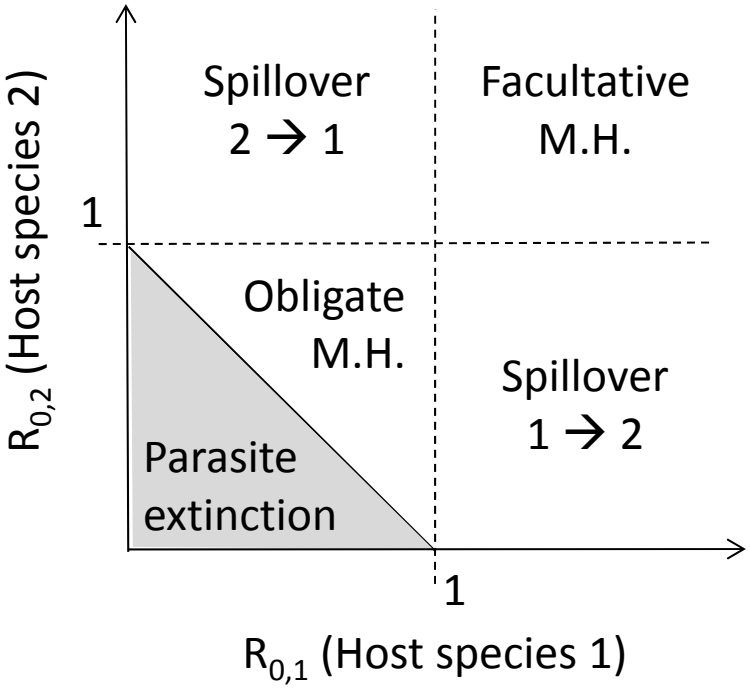
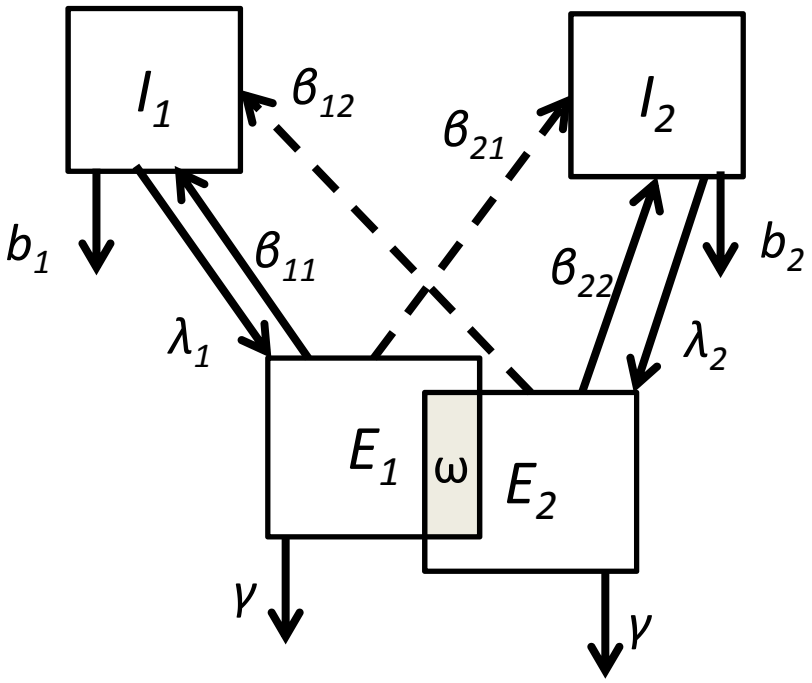

Spillover
2 → 1
Facultative
M.H.
1
Obligate
M.H.
Spillover
1 → 2
Parasite
extinction
1
$R_{0,2}$ (Host species 2)
$R_{0,1}$ (Host species 1)

Fig 2

A)


I_1
β_{12}
β_{21}
I_2
b_1
β_{11}
β_{22}
b_2
λ_1
λ_2
E_1
ω
E_2
γ
γ

B)

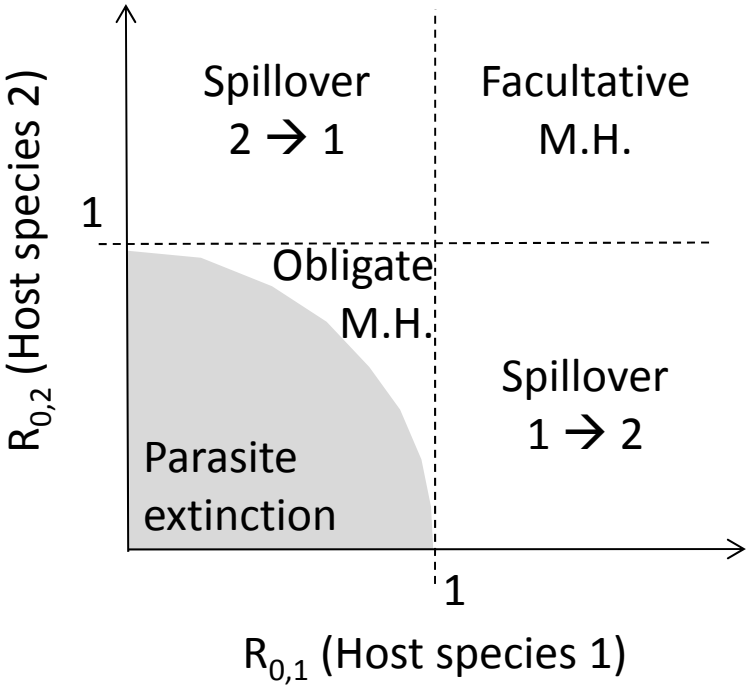

Spillover
2 → 1
Facultative
M.H.
1
Obligate
M.H.
Spillover
1 → 2
Parasite
extinction
1
$R_{0,2}$ (Host species 2)
$R_{0,1}$ (Host species 1)

Fig 3

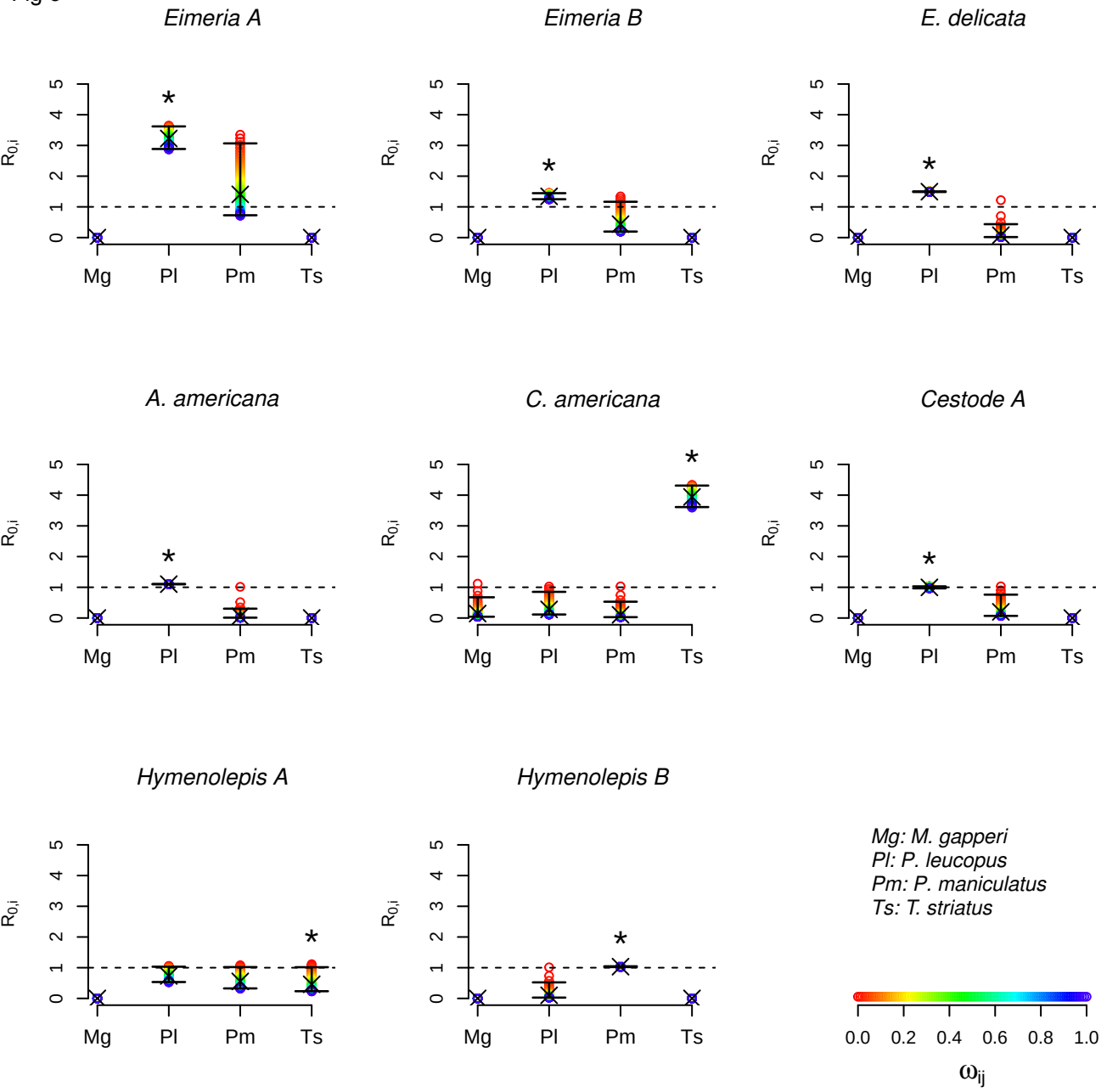
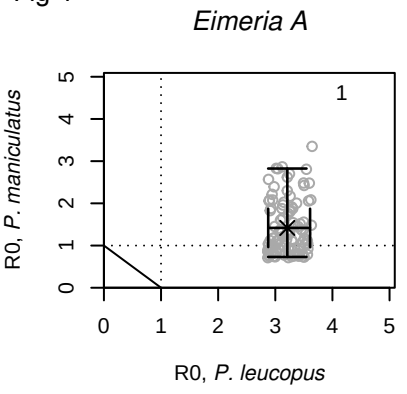
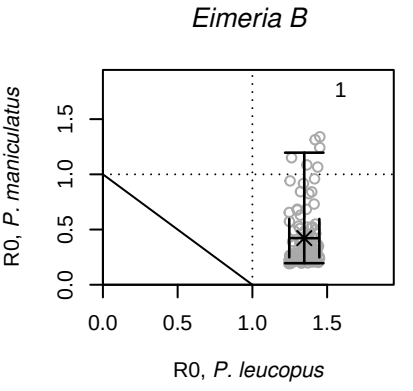
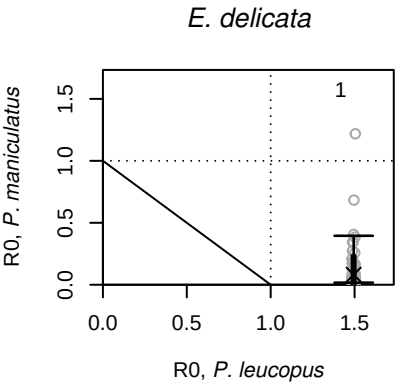
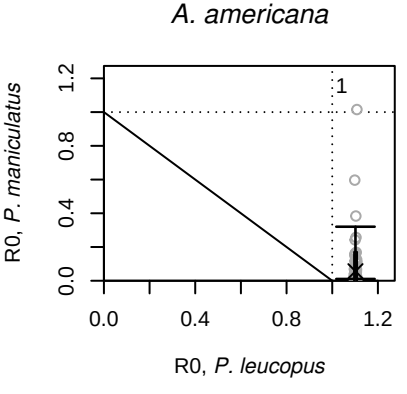

Eimeria A
Eimeria B
E. delicata
A. americana
C. americana
Cestode A
Hymenolepis A
Hymenolepis B
$R_{0,i}$
0 1 2 3 4 5
Mg Pl Pm Ts
*
Mg: M. gapperi
Pl: P. leucopus
Pm: P. maniculatus
Ts: T. striatus
0.0 0.2 0.4 0.6 0.8 1.0
ω_{ij}

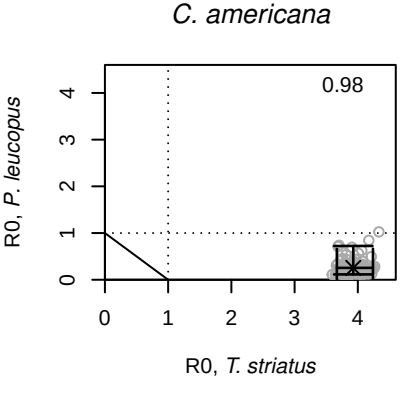
Fig 4

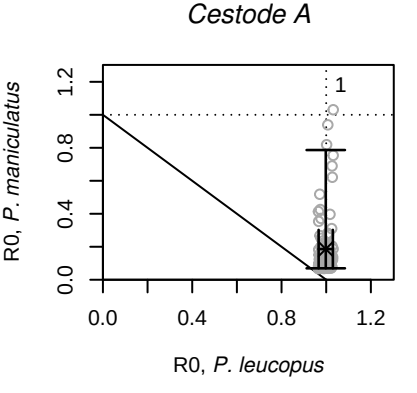

Eimeria A
1
R0, P. maniculatus
R0, P. leucopus

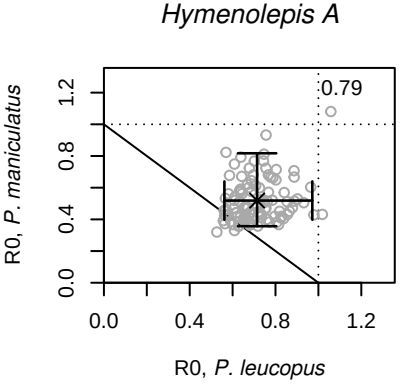

Eimeria B
1
R0, P. maniculatus
R0, P. leucopus


E. delicata
1
R0, P. maniculatus
R0, P. leucopus


A. americana
1
R0, P. maniculatus
R0, P. leucopus


C. americana
0.98
R0, P. leucopus
R0, T. striatus


Cestode A
1
R0, P. maniculatus
R0, P. leucopus


Hymenolepis A
0.79
R0, P. maniculatus
R0, P. leucopus

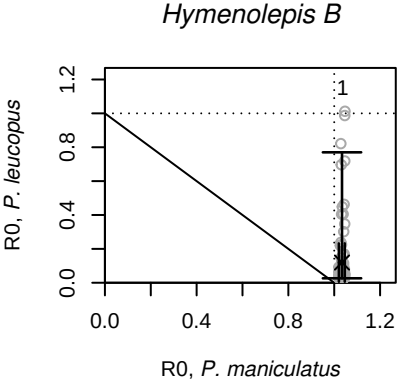
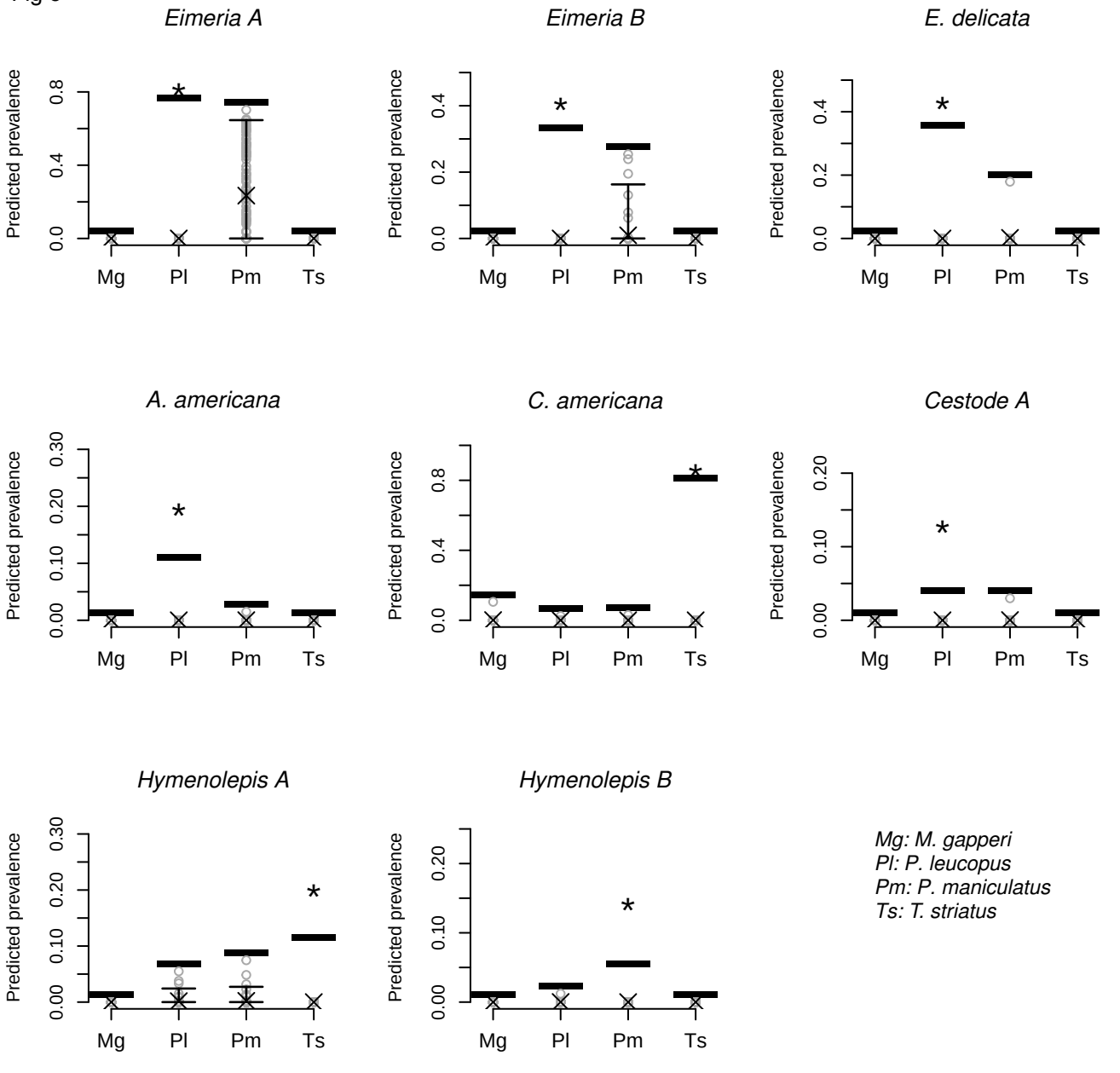
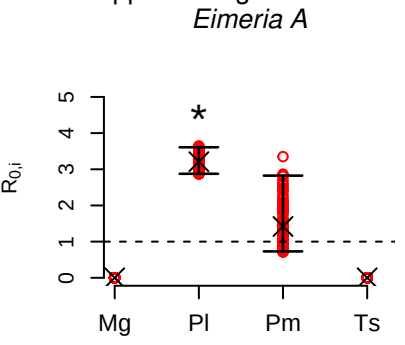
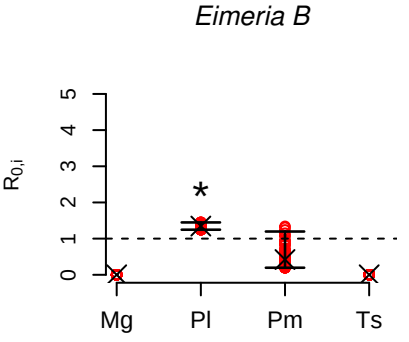

Hymenolepis B
1
R0, P. leucopus
R0, P. maniculatus

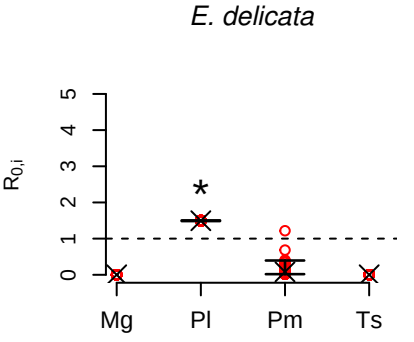
Fig 5

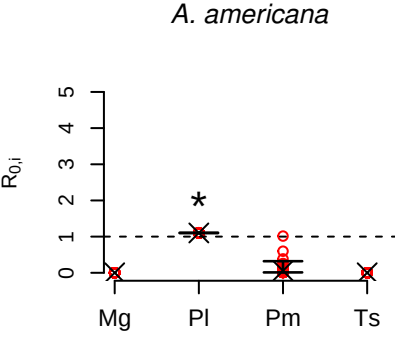

Eimeria A
Eimeria B
E. delicata
A. americana
C. americana
Cestode A
Hymenolepis A
Hymenolepis B
Predicted prevalence
Mg
Pl
Pm
Ts
Mg: M. gapperi
Pl: P. leucopus
Pm: P. maniculatus
Ts: T. striatus

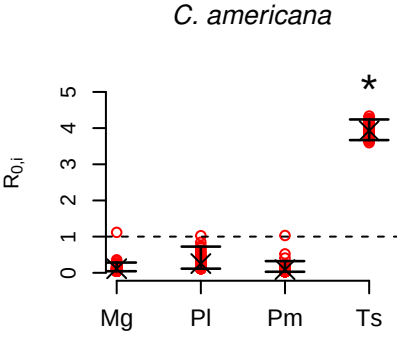
Online appendix Figures

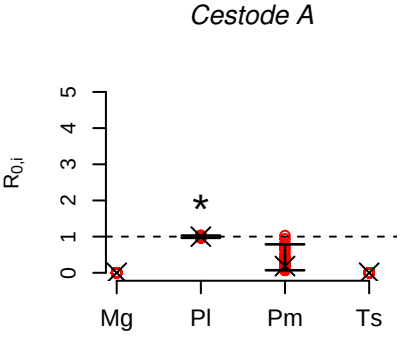


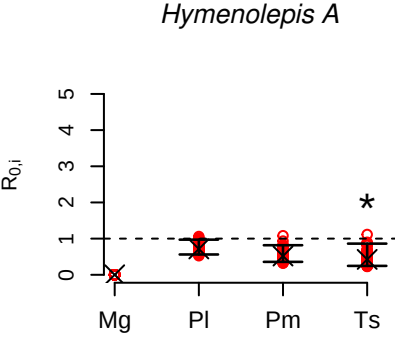


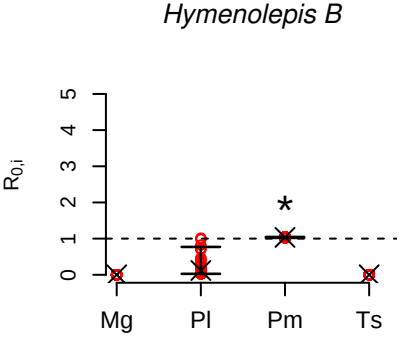












Mg: M. gapperi
Pl: P. leucopus
Pm: P. maniculatus
Ts: T. striatus

Fig A2

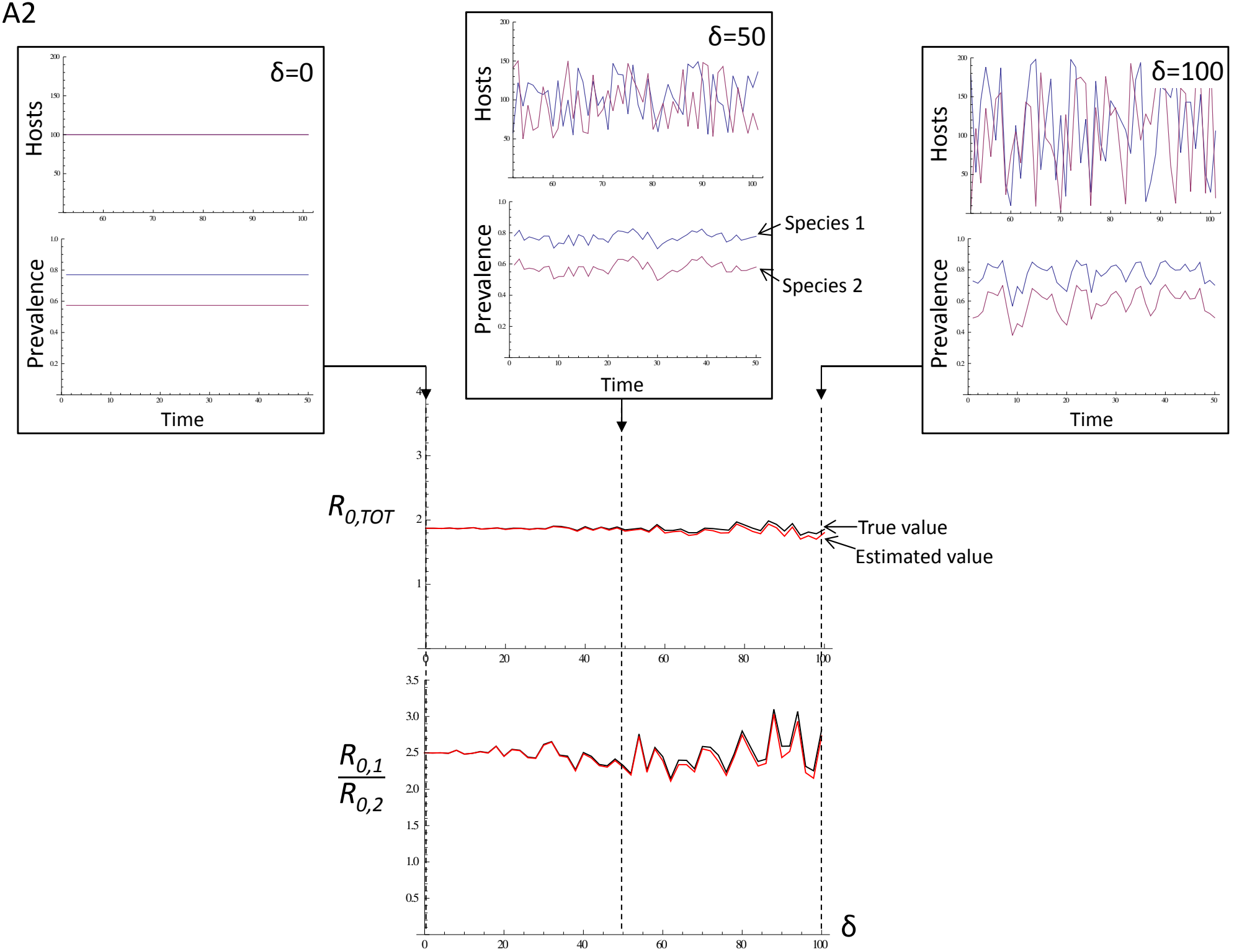

δ=0
Hosts
Prevalence
Time
δ=50
Hosts
Prevalence
Species 1
Species 2
Time
δ=100
Hosts
Prevalence
Time
$R_{0,TOT}$
True value
Estimated value
$\frac{R_{0,1}}{R_{0,2}}$
δ

Fig A3

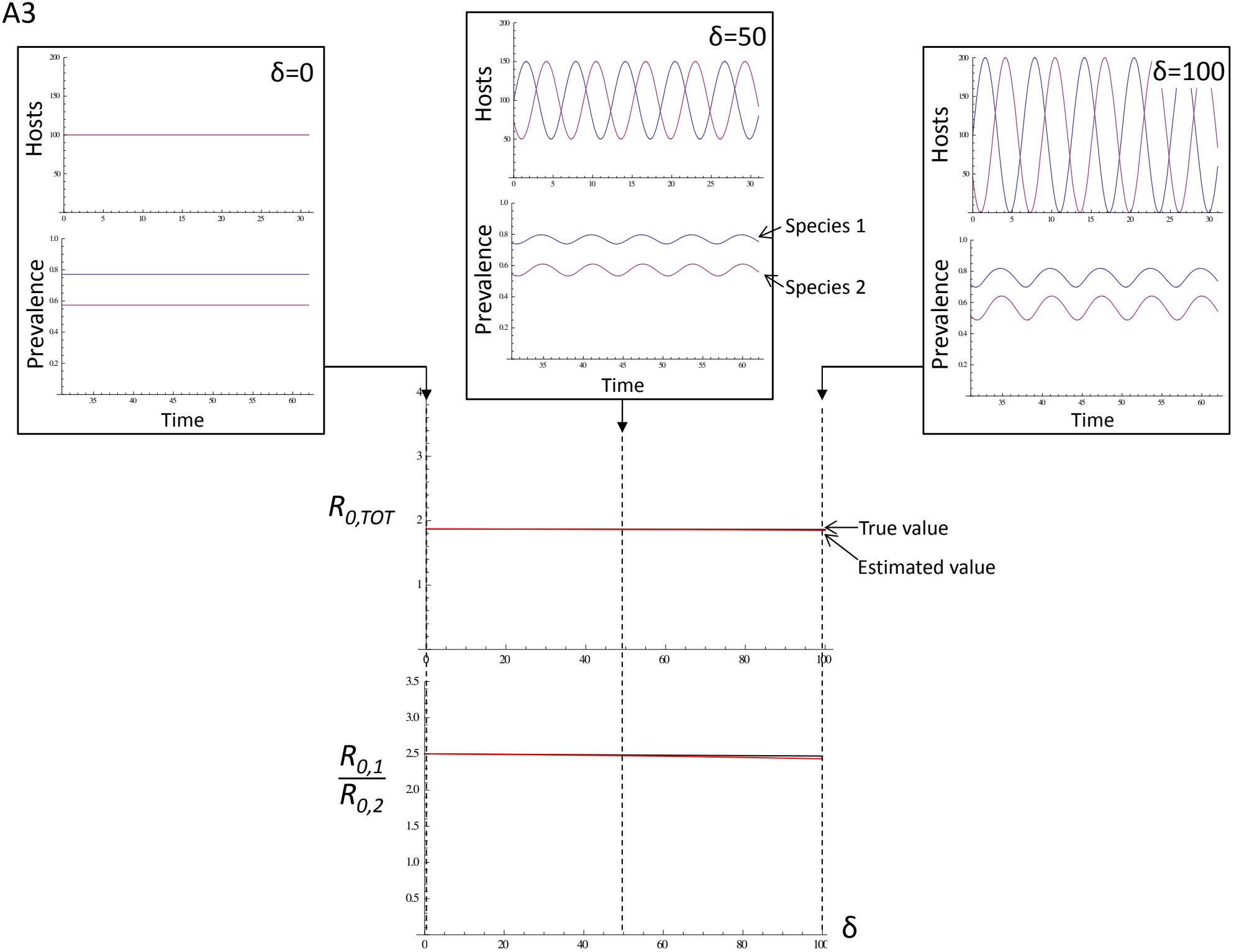
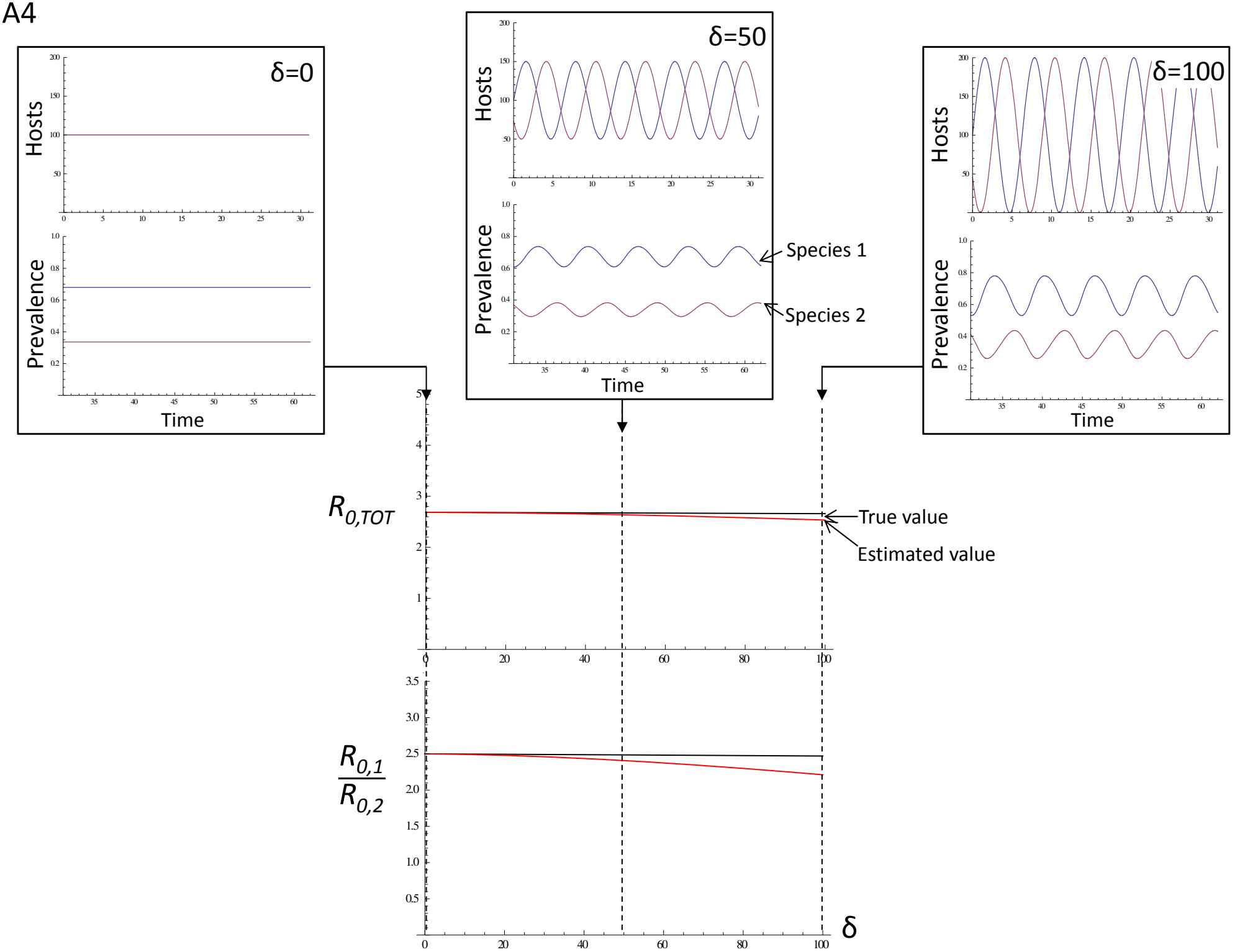

δ=0
δ=50
δ=100
Hosts
Prevalence
Time
Species 1
Species 2
$R_{0,TOT}$
True value
Estimated value
$\frac{R_{0,1}}{R_{0,2}}$
δ

Fig A4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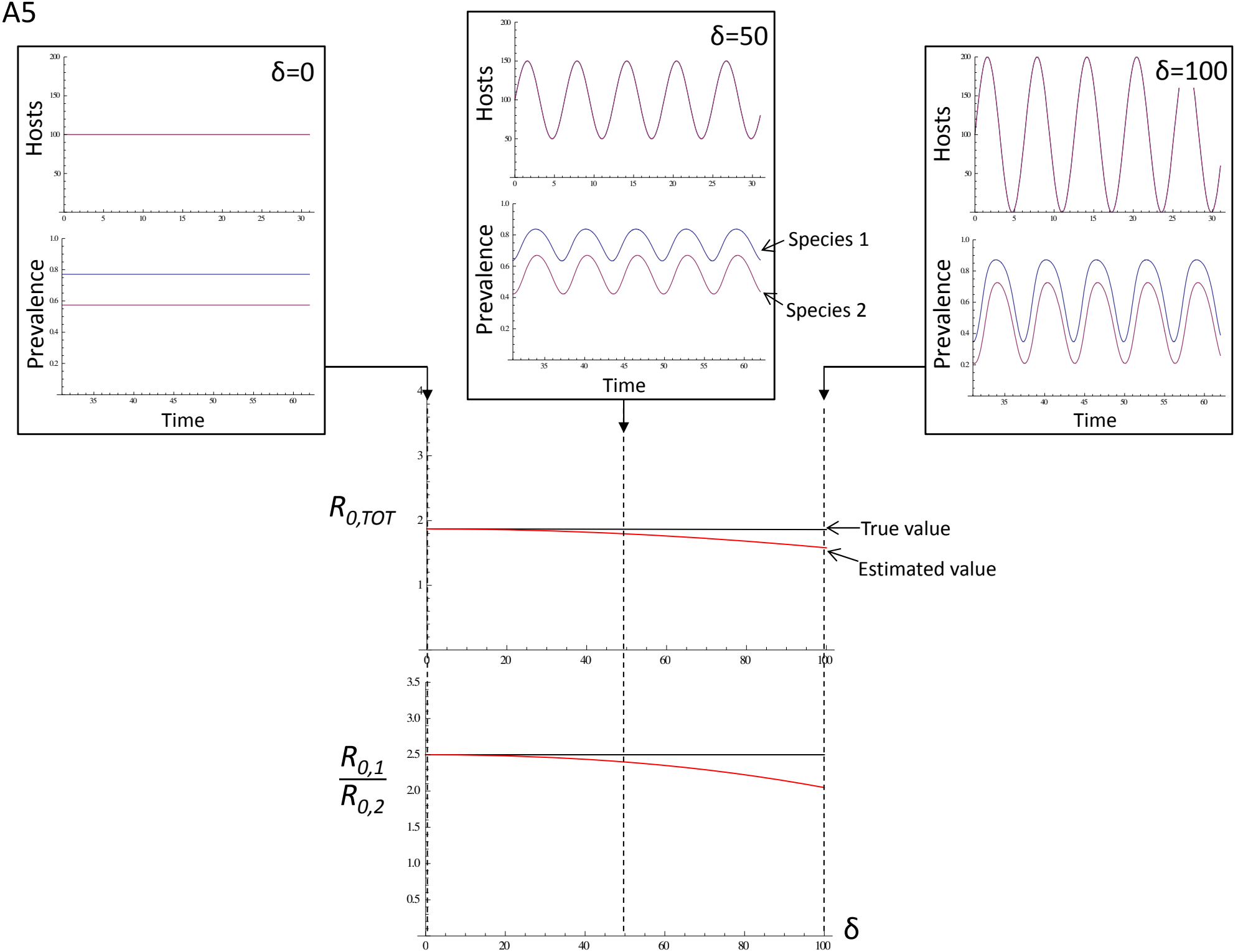
δ=50
δ=100
Hosts
Prevalence
Time
Species 1
Species 2
$R_{0,TOT}$
True value
Estimated value
$\frac{R_{0,1}}{R_{0,2}}$
δ

Fig A5


δ=0
δ=50
δ=100
Hosts
Prevalence
Time
Species 1
Species 2
$R_{0,TOT}$
True value
Estimated value
$\frac{R_{0,1}}{R_{0,2}}$
δ